

AMENDED CLAIMS +
STATEMENT UNDER ARTICLE 19(1)

10/588626

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[Received by the International Bureau on 21 November 2005 (21.11.05);
original claims 1-28 amended; new claims 1-27 added (4 pages)]

- 5 1. A method of damaging target cells in a subject, the method comprising administering to the subject
- (1) a nucleic acid encoding a compound capable of converting a substrate to acetaldehyde, wherein said compound is an enzymatically active portion of alcohol dehydrogenase; and
- 10 (2) a substrate which is converted to acetaldehyde by the portion capable of converting said substrate to acetaldehyde;
- wherein said substrate is ethanol.
- 15 2. A method according to claim 1 further comprising administering a component that is capable of inhibiting aldehyde dehydrogenase.
3. A method according to claim 2 wherein said component that is capable of
- 20 inhibiting aldehyde dehydrogenase is Disulfiram.
4. A method according to any of claims 1 to 3 wherein the nucleic acid is in the form of a viral vector.
- 25 5. A method according to claim 4 wherein the viral vector is a DNA based viral vector.
6. A method according to claim 5 wherein the DNA based viral vector is an adenovirus derived viral vector.
- 30 7. A method according to any of claims 1 to 6 wherein the nucleic acid comprises a polynucleotide comprising a target cell-specific promoter operably linked to a polynucleotide encoding said alcohol dehydrogenase.

8. A method according to any preceding claim in which the portion of alcohol dehydrogenase converts the ethanol to acetaldehyde as a result of its enzymatic activity.
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9. A method according to any of claims 4 to 8 wherein said vector comprises a target cell specific portion.
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10. A method according to according to claim 9 in which the target cell specific portion comprises an antibody or part thereof.
11. A method according to according to claim 9 or claim 10 in which the target-cell specific portion is capable of selectively binding to a cell surface entity.
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12. A method according to claim 11 in which the cell surface entity is a tumour-associated antigen.
13. A method according to any one of claims 9 to 12 in which the target cell specific portion comprises a liposome.
- 20
14. A method according to any one of claims 1 to 13 in which a radiation therapy is also administered to the subject.
- 25
15. A composition comprising a compound as defined in any of claims 1 to 13, wherein the portion of alcohol dehydrogenase is an enzymatically active portion of human alcohol dehydrogenase.
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16. A composition according to claim 16 wherein said human alcohol dehydrogenase is alcohol dehydrogenase $\beta 2$.
17. A composition according to claim 15 or claim 16 further comprising a substance which is capable of inhibiting aldehyde dehydrogenase.

18. A composition according to claim 17 wherein said substance which is capable of inhibiting aldehyde dehydrogenase is Disulfiram.
- 5 19. A composition according to any of claims 15 to 18 further comprising a chemotherapeutic agent.
20. A composition according to any of claims 15 to 19 further comprising an immunosuppressive agent.
- 10 21. A composition according to any of claims 15 to 20 for use in medicine.
22. Use of a composition according to any of claims 15 to 20 in the manufacture of a medicament for the treatment of cancer.
- 15 23. Use of ethanol or pyruvate in the manufacture of a medicament for the treatment of cancer.
- 20 24. A therapeutic system or kit comprising a compound or system as defined in any of claims 1-13, or a composition as defined in any of claims 15 to 20, and a second component which comprises ethanol, and optionally a third component that is capable of inhibiting aldehyde dehydrogenase.
- 25 25. A therapeutic system or kit according to claim 24 in which the aldehyde producing portion is a catalytically active portion of alcohol dehydrogenase, the second component is ethanol and the third component is Disulfiram.
- 30 26. Human alcohol dehydrogenase or a catalytically active portion thereof for use in medicine.
27. Use of alcohol dehydrogenase or a catalytically active portion thereof in the manufacture of a medicament for the treatment of cancer.

Statement Under Article 19(1)**PCT Patent Application No. PCT/GB2005/000363**

The amended claim set finds basis in the application as originally filed, in particular in the claims of the application as originally filed. The amended claims do not add matter to the application.

Original claims 27 and 28 have now been combined to form claims 1-6. Furthermore, these claims are now limited so that the compound capable of converting a substrate to acetaldehyde is an enzymatically active portion of alcohol dehydrogenase. Furthermore, the claims have been correspondingly limited so that the substrate is ethanol. Basis for these amendments may be found in the claims as originally filed, for example claim 9, and in the description of the application as originally filed.

Original claims 3, 9, 10, 11, 12 and 17 have all been deleted.

The remaining claims have each been retained, with appropriate amendment to reflect the limitations made in claim 1 involving alcohol dehydrogenase and ethanol.

Furthermore, the claims have been amended to remove occurrences of terms such as "preferably" and "optionally", presenting the preferred or optional features as dependent claims where appropriate.